

### **AMENDMENTS TO THE CLAIMS**

The following listing of the claims replaces all prior versions of the claims presented in the application.

1. (Previously presented) A recombinant mutant allergen of a naturally occurring allergen,

said naturally occurring allergen selected from the group consisting of Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens and comprising at least four mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen,

each of said at least four mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates,

each of said at least four mutations being spaced from each other by at least 15 Å,  
and

said mutant allergen comprising at least one circular surface region with a area of 800 Å<sup>2</sup> that comprises no mutation.

2. (Previously presented) A recombinant mutant allergen according to claim 1, wherein the each of said at least four mutations is spaced from each other by between about 20 to 30 Å.

3. (Previously presented) A recombinant mutant allergen according to claim 1 which comprises at least five mutations in total, which each reduces the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen,

each of said at least five mutations in total being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the

amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and

at least two of said at least five mutations in total being spaced within 15 Å of each other.

4. (Previously presented) A recombinant mutant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 20 %.

5. (Previously presented) A recombinant mutant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

6. (Previously presented) A recombinant mutant allergen according to claim 1, which essentially has the same  $\alpha$ -carbon backbone tertiary structure as said naturally occurring allergen.

7. (Previously presented) A recombinant mutant allergen according to claim 1, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic genus from which said naturally occurring allergen originates.

8. (Previously presented) A recombinant mutant allergen according claim 1, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 5%.

9. (Previously presented) A recombinant mutant allergen according to claim 6, characterised in that when comparing the  $\alpha$ -carbon backbone tertiary structures of the mutant and

the naturally occurring allergen molecules, the average root mean square deviation of the atomic coordinates is below 2Å.

10. (Previously presented) A recombinant mutant allergen according to claim 1, characterised in said circular surface region comprises atoms of 15-25 amino acid residues.

11. (Previously presented) A recombinant mutant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to solvent accessibility, and that one or more amino acids among the more solvent accessible ones are substituted.

12. (Previously presented) A recombinant mutant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to degree of conservation in all known homologous proteins within the species from which said naturally occurring allergen originates, and that one or more amino acids among the more conserved ones are substituted.

13. (Previously presented) A recombinant mutant allergen according to claim 1, wherein the mutant allergen is a non-naturally occurring allergen.

14. (Previously presented) A recombinant mutant allergen according to claim 1 comprising from 5 to 20 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen,

each of said 5 to 20 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and

each of said 5 to 20 mutations being spaced from each other by at least 15 Å.

15. (Previously presented) A recombinant mutant allergen according to claim 3, which comprises at least 8 total mutations and wherein each of said at least four mutations spaced from each other by at least 15 Å is spaced within 15 Å of 1 to 4 of said at least 8 total mutations.

16. (Withdrawn/Previously presented) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a grass group 5 allergen selected from the group consisting of Lol p 5, Phl p 5, Poa p 5 and Sec c 5.

17. (Previously presented) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a house dust mite group 2 allergen selected from the group consisting of Der p 2, Der f 2 and Lep d 2.

18. (Withdrawn/Previously presented) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a Fagales group I allergen selected from the group consisting of Bet v 1, Aln g 1, Cor a 1 and Car b 1.

19. (Withdrawn/Previously presented) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a Vespidae antigen 5 allergen selected from the group consisting of Ves v 5 and Pol a 5.

20. (Withdrawn/Previously presented) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a house dust mite group 1 allergen selected from the group consisting of Der p 1, Derf f 1 and Lep d 1.

21. (Withdrawn/Previously presented) A recombinant mutant allergen according to claim 18, characterised in that it is a mutant of Bet v 1.

22. (Withdrawn/Previously presented) A recombinant mutant allergen according to claim 21, characterised in that one or more of the substitutions is selected from the group consisting of V-2, D-72, E-87, K-129, E-60, N-7, K-65, P-108, N-159, D-93, K-123, K-32, D-125, R-145, D-

109, E-127, Q-36, E-131, L-152, E-6, E-96, D-156, P-63, H-76, E-8, K-134, E-45, T-10, V-12, K-20, S-155, H-126, P-50, N-78, K-119, V-2, L-24, E-42, N-4, A-153, I-44, E-138, G-61, A-130, R-70, N-28, P-35, S-149, K-103, Y-150, H-154, N-43, A-106, K-115, P-14, Y-5, K-137, E-141, E-87 and E-73.

23 -34. (Cancelled)

35. (Previously presented) A pharmaceutical composition comprising the recombinant mutant allergen according to claim 1 and at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

36. (Cancelled)

37. (Previously presented) A composition comprising two or more recombinant mutant allergens according to claim 1, wherein each of said two or more recombinant mutant allergens respectively comprises at least one-mutation among said at least four mutations spaced at least 15 Å from each other that is at least 15 Å from any other mutation that is absent in at least one other of said two or more recombinant mutant allergens.

38. (Previously presented) A composition according to claim 37 comprising 2-12 recombinant mutant allergens.

39. (Previously presented) A composition according to claim 37 further comprising at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

40-65. (Cancelled)

66. (Previously presented) The recombinant mutant allergen of claim 2 wherein said at least four mutations are spaced from each other by at least 25 Å.

67. (Currently amended) The recombinant mutant allergen of claim ~~[[66]]~~ 1 wherein said at least four mutations are spaced from each other by at least 30 Å.

68. (Previously presented) The recombinant mutant allergen according to claim 4, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 30 %.

69. (Previously presented) The recombinant mutant allergen according to claim 68, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 40 %.

70. (Previously presented) The recombinant mutant allergen according to claim 69, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 50 %.

71. (Previously presented) A recombinant mutant allergen according to claim 5, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 80 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

72. (Previously presented) A recombinant mutant allergen according to claim 71, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 90 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

73. (Previously presented) A recombinant mutant allergen according to claim 7, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic subfamily from which said naturally occurring allergen originates.

80. (Previously presented) A recombinant mutant allergen according to claim 14 comprising from 6 to 15 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen,

each of said 6 to 15 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and

each of said 6 to 15 mutations being spaced from each other by at least 15 Å.

81. (Previously presented) A recombinant mutant allergen according to claim 80 comprising from 7 to 12 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen,

each of said 7 to 12 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and

each of said 7 to 12 mutations being spaced from each other by at least 15 Å.

82. (Previously presented) A recombinant mutant allergen according to claim 81 comprising from 8 to 10 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen,

each of said at said 8 to 10 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and

each of said 8 to 10 mutations being spaced from each other by at least 15 Å.

83. (Previously presented) A composition according to claim 38 comprising 3-10 recombinant mutant allergens.

74. (Previously presented) A recombinant mutant allergen according to claim 73, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic family from which said naturally occurring allergen originates.

75. (Previously presented) A recombinant mutant allergen according to claim 74, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic superfamily from which said naturally occurring allergen originates.

76. (Previously presented) A recombinant mutant allergen according to claim 75, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic legion from which said naturally occurring allergen originates.

77. (Previously presented) A recombinant mutant allergen according to claim 76, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic suborder from which said naturally occurring allergen originates.

78. (Previously presented) A recombinant mutant allergen according to claim 77, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic order from which said naturally occurring allergen originates.

79. (Previously presented) A recombinant mutant allergen according claim 8, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 10%.



84. (Previously presented) A composition according to claim 83 comprising 4-8 recombinant mutant allergens.

85. (Previously presented) A composition according to claim 84 comprising 5-7 recombinant mutant allergens.